NDA 18-723/S-028
NDA 19-680/S-014
NDA 20-593/S-002
NDA 18-081/S-032
NDA 18-082/S-023

JUN 19 2000

Abbott Laboratories
Attention: James D. Steck
Director, PPD Regulatory Affairs
100 Abbott Park Road
D-491, AP6B-1SW
Abbott Park, Illinois 60064-6108

Dear Mr. Steck:

Please refer to the following supplemental new drug applications submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Depakote Tablets (divalproex sodium delayed release tablets), Depakote Sprinkle Capsules (divalproex sodium coated particles in capsules), Depacon Injection (valproate sodium injection), Depakene Capsules (valproic acid capsules, USP), and Depakene Syrup (valproic acid syrup, USP).

	Initial Submission	Response to Action Letter	Additional Amendment
NDA 18-723/S-028	June 15,1999	February 23,2000	April 5,2000
NDA 19-680/S-014	September 13,1999	April 5,2000	
NDA 20-593/S-002	September 13, 1999	April 5,2000	
NDA 18-081/S-032	September 13,1999	May 26,2000	
NDA 18-082/S-023	September 13,1999	May 26,2000	

These "Changes Being Effected" supplemental new drug applications provide for addition of the following new safety information to the labeling of these products:

1. Statements in the PRECAUTIONS and ADVERSE REACTIONS sections of labeling regarding a valproate/amitriptyline/nortriptyline drug interaction, anaphylaxis, parkinsonism, and effects of valproate on HIV replication.

2. Information in the WARNINGS section and in the Geriatric subsection of the PRECAUTIONS and DOSAGE AND ADMINISTRATION sections of labeling regarding somnolence in the elderly.

3. Statements in the Box Warning and WARNINGS section of labeling regarding pancreatitis.

We have completed the review of these supplemental applications, as amended, and have concluded that adequate information has been presented to demonstrate that the drug products are safe and effective for use as recommended in the agreed upon enclosed labeling text. Accordingly, these supplemental applications are approved effective on the date of this letter.

Please note that the following revisions have been made to labeling since your last submissions:

1. The word "a" has been deleted from the 1st sentence in the 2nd paragraph of the CLINICAL TRIALS/Epilepsy section in the Depakote Tablet, Depakote Sprinkle Capsules, and Depakene Capsule and Syrup package inserts.

2. The word "vasodilation" has been added to the ADVERSE REACTIONS/Mania/ Cardiovascular section in the Depacon package insert.

3. The "Pediatric" and "Geriatric" subheaders in the PRECAUTIONS section have been revised to "Pediatric Use" and "Geriatric Use" in all four package inserts.

4. The word "an" has been added to the last sentence (in front of "increase") of the Mutagenicity subsection in the PRECAUTIONS section in the Depakote Tablet, Depakote Sprinkle Capsules, and Depakene Capsule and Syrup package inserts.

5. The 2nd sentence of the 1st paragraph of the DOSAGE AND ADMlNISTRATION/Epilespy section has been replaced with the following sentence, " DEPAKOTE is indicated as monotherapy and adjunctive therapy in complex partial seizures in adults and pediatric patients down to the age of 10 years, and in simple and complex absence seizures." in the Depakote Tablet and Depakote Sprinkle Capsules package inserts.

6. The reference to (15-25°F) has been corrected to (15-25°C) in the HOW SUPPLIED section in the Depakene Capsule and Syrup package insert.

7. The word "children" has been changed to "pediatric patients" in the 1st sentence of the 1st paragraph of the PRECAUTIONS/Pediatric section in the Depacon package insert.

Lastly, several minor punctuation and spelling errors have been corrected.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert, text for the patient package insert).

Please submit 20 copies of the FPL as soon as it is available, in no case more than 30 days after it is printed to each application. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, these submissions should be designated "FPL for approved supplement NDA 18-723/S-028, 19-680/S-014,20-593/S-002, 18-081/S-032, 18-082/S-023." Approval of these submissions by FDA is not required before the labeling is used.

In addition, please note that we have reviewed the content of the following supplements submitted as "changes being effected," and we note that these changes have been incorporated in the enclosed labeling text. Therefore, the supplemental applications listed below have been superceded, and will be retained in our files with no further action.

Supplement Number:	Date Submitted:
NDA 18-723/S-023	February 26,1997
NDA 19-680/S-012	February 26,1994

We remind you that the Dear Health Care Professional letter is to be mailed utilizing the "Important Drug Warning" statement and red rectangular border as described under 21 CFR 200.5. We also ask that you consider utilizing this statement (and its border) on the first page of the Dear Health Care Professional letter in the upper right hand corner.

Additionally, we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.